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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,703	06/27/2000	IAN ROSS DOYLE	13704/2	9876

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KENYON & KENYON LLP
ONE BROADWAY
NEW YORK, NY 10004

EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
11/23/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/486,703	DOYLE ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 6-15-2010 has been entered.

Claims 51-72 are pending and under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Maintained

Claims 51-64 stand rejected under 35 U.S.C. 102(b) as being anticipated by Doyle et al (Advances in Critical Care Testing, Eds. Muller and McQueen, Springer-Verlag Telos, January 1997; reference A17 on the PTOL-1449 of 10-18-00) for all the reasons made of record and those herein.

The teachings of Doyle et al are reiterated below.

Surfactant as a Marker of Disease Severity in Critically Ill Patients with Respiratory Failure

I. Doyle and A.D. Bersten

Introduction

Alveolar surfactant is fundamental for normal lung function. We recently reported increased concentrations of surfactant protein A (SP-A) in serum from patients with acute respiratory failure (ARF). Since surfactant protein B (SP-B) is synthesised as a precursor (approximately 42 kDa) considerably smaller than alveolar (a) SP-A (approximately 650 kDa) and since little is known about surfactant status in patients with ARF, the aims of this study were to determine whether SP-B enters the circulation more readily than SP-A and to examine surfactant composition in the injured lung.

Methods

Blood was collected from normal individuals (controls) and from ventilated patients with either no evidence of cardiorespiratory disease (OD), acute cardiogenic pulmonary oedema (APE) or acute respiratory distress syndrome (ARDS). Surfactant composition in tracheal aspirate fluid (ASF) was examined in a separate cohort of patients, either with, or at risk of, ARDS. SP-A and B were measured by enzyme-linked immunosorbent assay (ELISA). ASF phospholipids and disaturated phospholipids (DSP) were measured and phospholipid classes quantified by high-performance liquid chromatography (HPLC). All analyses were performed in a randomised, blind manner.

Results

Plasma SP-A and SP-B levels at enrolment are shown in Table 1. Plasma SP-A and SP-B levels were elevated in the APE and ARDS patients relative to the controls and OD patients ($p<0.001$ in all comparisons, Mann-Whitney test). During the course of their admission, plasma SP-A and SP-B were inversely related to blood oxygenation (PaO_2/FiO_2; $p<0.0001$, $n=260$; Spearman) and static respiratory system compliance ($\Delta V/\Delta P$; $p<0.0001$, $n=168$). Plasma SP-B/SP-A was also inversely related to PaO_2/FiO_2 ($p<0.026$) and $\Delta V/\Delta P$

Table 1. Plasma surfactant protein A (SP-A) and SP-B levels at enrolment (mean±SE)

Plasma	Controls ($n=33$)	OD ($n=7$)	APE ($n=10$)	ARDS ($n=22$)
SP-A (ng/ml)	17±37	177±16	261±22	478±58
SP-B (ng/ml)	3685±58	1629±633	3846±635	8007±1654

OD, patients with no evidence of cardiorespiratory disease; APE, patients with acute cardiogenic pulmonary oedema; ARDS, patients with acute respiratory distress syndrome.

Table 2. Correlations

	PaO_2/FiO_2	Eprv-st	Ers-dyn	$\%E_2$
Alv SP-A	0.73*	0.85**	−0.06	−0.65*
Alv SP-B	0.74*	0.68**	−0.08	−0.54**
DSP	0.67*	0.56**	−0.21	−0.73*
PC	0.65*	0.61**	0.03	−0.67*
SPH/PL	−0.64*	−0.54**	−0.06	0.68*

Eprv-st, static elastance of the positive end-expiratory pressure (PEEP)-recruited volume; Ers-dyn, dynamic respiratory elastance; $\%E_2$, volume-dependent component of Ers-dyn; SP, surfactant protein; DSP, disaturated phospholipids; PC, phosphatidylcholine; SPH, sphingomyelin.
* $p<0.01$; ** $p<0.05$.

($p<0.009$). Individually, daily changes in lung function were acutely reflected in concomitant variations in plasma SP-A, SP-B and SP-B/SP-A.

When normalised to sphingomyelin (SPH), alveolar SP-A and SP-B, DSP and phosphatidylcholine (PC) correlated directly with PaO_2/FiO_2 and static elastance of the positive end-expiratory pressure (PEEP)-recruited volume (Eprv-st), whereas SPH/PL was inversely related to both. When dynamic respiratory elastance (Ers-dyn; 1/compliance) and its volume-dependent component ($\%E_2$), representing lung hyperinflation, were determined; alveolar SP-A and SP-B, DSP and PC were inversely related to $\%E_2$, whereas SPH/PL was directly related. The correlation values for these various relationships are shown in Table 2.

Conclusions

We concluded that SP-B enters the circulation more readily than SP-A in a manner reflecting the severity of lung injury and that surfactant deficiency is a major factor contributing to hypoxaemia and lung hyperinflation in ARF.

Doyle et al teach normal individuals (controls) and ventilated patients with no evidence of cardiorespiratory disease (OD) . Doyle et al teach that these individuals were screened for plasma levels of surfactant protein B (SP-B) (see Table 1). Applicant and Declarant argue that the patient populations of Doyle et al do not meet the patient

population of asymptomatic or when the clinical diagnosis of lung damage in the mammal cannot otherwise be confirmed without the aid of one or more invasive procedures. This is not persuasive for all the reasons already made of record. Declarant indicates that the precise physical characteristics of the patients in the populations are not set forth. This is not persuasive because Doyle et al specifically teach that the control individuals were "normal individuals" and the OD patients had no evidence of cardiorespiratory disease. As such, in contrast to Declarant's and Applicants response, Doyle et al does in fact characterize the patient populations with particular specificity. Declarant sets forth the position that the patient population would not be consistent with the interpretation of the examiner and that set forth in Doyle et al because the skilled artisan would necessarily have preformed a high degree of inquiry including asking pertinent questions being asked by the clinician in the course of the clinician's evaluation of relevant criteria in assessing lung health. This is not persuasive as is it clearly a narrower interpretation not supported by the specification. The specification does not describe that the patients were selected based on extensive questioning by a clinician and does not set forth this as the definition of the recited patient populations of asymptomatic or when the clinical diagnosis of lung damage in the mammal cannot otherwise be confirmed without the aid of one or more invasive procedures. During patent examination, the claims are given the broadest reasonable interpretation consistent with the specification. See *In re Morris*, 127 F.3d 1048, 44 USPQ2d 1023 (Fed. Cir. 1997). Declarant also indicates that one skilled in this art would not see the ventilated patients with no evidence of cardiorespiratory disease (OD) as meeting the limitation of when the clinical diagnosis of lung damage in the mammal cannot otherwise be confirmed without the aid of one or more invasive procedures. Declarant argues that one skilled in the art would not interpret the teachings of Doyle et al as did the office Because other published authors have labeled subjects as having "the absence of respiratory complaints", when in fact subsequent inquiry established that they did have symptoms of cardiorespiratory disease and/or lung damage. This is not

persuasive as this does not establish that the patients of Doyle et al did not meet the criteria of the claims. Declarant argues that an individual could fall within the normal or OD group of Doyle et al, yet still not be within the scope of the patient populations of the pending claims. This is an erroneous interpretation of what is within the scope of the claims. Declarant speculates that if Doyle used the same criteria as that of Remy-Jardin et al then such an individual would be placeable within the normal or OD groups of Doyle, yet not fall within the patient populations of the current claims. This is again not persuasive as the claims do not require Applicants narrow definitions and Doyle et al does not teach that they used the criteria of Remy-Jardin. In contrast to Declarant's position, the lack of specific definition of the terms or the patient populations, the terms do not exclude the patients of Doyle et al and Doyle et al specifically and particularly characterize the patient populations such that they would necessarily fall within the claimed patient populations. The Office has properly shifted burden to Applicant.

It is also noted for the record that the "wherein" clause recited in claims 65-72 ("wherein an increase in the levels of SP-B relative to the normal reference level is indicative of lung damage"), the clause does not recite any additional active method steps, but simply states a characterization or conclusion of the results of those steps. Therefore, the "wherein" clause is not considered to further limit the method defined by the claim and has not been given weight in construing the claims. See *Texas Instruments, Inc. v. International Trade Comm.*, 988 F.2d 1165, 1171, 26 USPQ2d 1018, 1023 (Fed Cir. 1993) ("A 'whereby' clause that merely states the result of the limitations in the claim adds nothing to the patentability or substance of the claim."). See also *Minton v. National Assoc. of Securities Dealers, Inc.*, 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003) ("A whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.").

Although the reference is silent about alveolar-capillary membrane damage, it does not appear that the claim language or limitations result in a manipulative difference in the

method steps when compared to the prior art disclosure. See *Bristol-Myers Squibb Company v. Ben Venue Laboratories* 58 USPQ2d 1508 (CAFC 2001). {i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable. *In re Woodruff*, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. *In re Baxter Travenol Labs,* 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

Claims 51-72 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Doyle et al Am. J. Respir. Crit. Card. Med. 1994l 149;A576; of record hereinafter Doyle A.) in view of Doyle et al (Advances in Critical Care Testing, Eds. Muller and McQueen, Springer-Verlag Telos, January 1997; of record hereinafter Doyle B), Doyle et al (Am. J. Respir. Crit. Care. Med. 152:307-317, 1995; of record hereinafter Doyle C), Honda (Japanese Journal of Thoracic Diseases, 34 Suppl. Abstract only, December 1996; of record) and Abe et al (Japanese Journal of Thoracic Diseases, 33(11):1219, Abstract only, November 1995; of record) for all the reasons made of record and those herein.

Applicants argue that since Doyle et al fails so does the rejection based upon Doyle et al. This is not persuasive because Doyle et al does not fail for all the reasons set forth and those of record herein.

Status of Claims

Claims 51-72 stand rejected.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the

grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 7:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor Larry Helms can be reached at 571-272-0832.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Patricia A. Duffy/

Primary Examiner